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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,856	01/30/2006	Heinz W. Gschwend	17243004001	2175

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EXAMINER	
JAISLE, CECILIA M	
ART UNIT	**PAPER NUMBER**
1624	

NOTIFICATION DATE	DELIVERY MODE
09/24/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docket@oshaliang.com
gourrier@oshaliang.com

Office Action Summary	Application No.	Applicant(s)	
	10/566,856	GSCHWEND ET AL.	
	Examiner	Art Unit	
	Cecilia M. Jaisle	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1--37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,15,36 and 37* is/are rejected.

7)☒ Claim(s) *12-14 and 16-35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01-30-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Lack of Unity

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions that are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 1-37, drawn to pyridazine derivatives, in which in the compounds of Formula (I), R^6, R^{6a}, R^7, R^{7a}, R^8, R^{8a}, R^9 and R^{9a} are each independently selected from hydrogen or C1-C3alkyl, classified in class 540, subclass 470, class 544, subclass 238, and their pharmaceutical compositions and methods, classified in class 514, subclass 218.

II. Claims 1-10, 36 and 37, drawn to pyridazine derivatives, in which in the compounds of Formula (I), R^6 and R^{6a} together, or R^7 and R^{7a} together, or R^8 and R^{8a} together, or R^9 and R^{9a} together are an oxo group, classified in class 540, subclass 460, class 544, subclass 238 and their pharmaceutical compositions and methods, classified in class 514, subclasses 218.

III. Claims 1-10, 36 and 37, drawn to pyridazine derivatives, in which in the compounds of Formula (I), R^6 or R^{6a} together or R^7 or R^{7a} together with one of R^8, R^{8a}, R^9 or R^{9a} form an alkylene bridge, classified in class 540, subclass 470,

class 544, subclasses 238, and their pharmaceutical compositions and methods, classified in class 514, subclasses 218.

Each group as set forth lacks unity with each other group, i.e., there is no single general inventive concept. The unique special technical features in each group are the identities of the Formula (I) compounds. The technical relationship among the inventions does not involve at least one common or corresponding special technical feature. The expression "special technical feature" means those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art. In this case, a reference that could be used to reject the compounds of Group I could not be used to reject the compounds of Groups II-III.

The Groups I and II inventions have special technical features not common to Groups III and would be expected to be useful other than as disclosed, e.g., to inhibit histone deacetylase enzymatic activity (WO 03/075929, cited in the specification).

During a telephone conversation with Dr. T. Chyau Liang on Aug. 22, 2007 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-37. Applicant must affirm this election in replying to this Office action. Claims 1-37 are under examination only to the extent that they are directed to the invention of Group I. Otherwise, claims 1-37 are withdrawn from examination to the extent that they are not directed to the invention of Group I.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Rejections under 35 US 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of stearoyl-CoA desaturase activity in mice, does not reasonably provide enablement for inhibiting human stearoyl-CoA desaturase activity (claim 1), for treating a disease or condition mediated by SCD in a mammal (claims 2,3 and 10) or for treating Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, fatty liver, non-alcoholic steatohepatitis, dyslipidemia or metabolic syndrome (claims 4-9). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Many factors require consideration when determining whether sufficient evidence supports a conclusion that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue." MPEP 2164.01(a). These factors include: (1) the claim breadth; (2) the nature of the invention; (3) the state of the prior art; (4) the level of predictability in the art; (5) the amount of direction provided by the

inventor; (6) the presence of working examples; and (7) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)(reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement). See also *In re Goodman* 29 USPQ2d 2010, 2013 (Fed. Cir. 1993). Application of these factors to the present application supports the determination that the present disclosure fails to satisfy the enablement requirement:

(1) Breadth of claims.

(a) Scope of the compounds. The claims cover potentially billions of pyridazines compounds of Formula (I).

(b) Scope of the diseases covered. The claims embrace treatment all diseases, including ones as yet undetermined, by inhibiting human stearoyl-CoA desaturase activity (claim 1), mediated by SCD in a mammal (claims 2,3 and 10), including Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, fatty liver, non-alcoholic steatohepatitis, dyslipidemia or metabolic syndrome (claims 4-9). Therefore, the claims are of unknown scope.

Current medical knowledge emphasizes that each specifically named disease/condition requires lifestyle changes, especially diet and exercise, for successful treatment. The major goal in treating Type II diabetes is to minimize blood sugar elevation without causing abnormally low blood sugar levels. Type II diabetes is treated first with weight reduction, diabetic diet, and exercise. When

these measures fail to control the elevated blood sugars, oral medications are used. If oral medications are still insufficient, treatment with insulin is considered.

Impaired Glucose Tolerance (IGT) is a pre-diabetic state dysglycemia, that is associated with insulin resistance and increased risk of cardiovascular pathology. Although some drugs can delay the onset of diabetes, lifestyle modifications play a greater role in the prevention of the disease. Patients identified as having an IGT should exercise regularly and have a balanced diet removing sugar.

Reducing insulin need and increasing cell sensitivity to the action of insulin is generally the management for insulin resistance. Recommended treatment involves dietary therapy, which should be low- or very-low calorie and low-fat, and physical activity, to maintain weight loss and reduce waist circumference.

Treatment of fatty liver disease depends on the underlying cause. If the underlying cause is high level of alcohol consumption, treatment includes limitation or elimination of alcohol consumption. If alcohol consumption is not the cause (non-alcoholic steatohepatitis or NASH), preferred treatments include weight loss and exercise, diabetes control, cholesterol control and avoidance of toxic substances, including alcohol and avoidance of medications and other substances that can cause liver damage.

Dyslipidemia requires lipid lowering with aggressive statin therapy, and combined therapy including bile acid resins, nictonic acid, fibrates and fish oil or omega-3 fatty acids.

An association between certain metabolic disorders and cardiovascular disease is known as metabolic syndrome; a clustering of risks leading to cardiovascular disease include insulin resistance, hypertension, cholesterol abnormalities, and an increased clotting risk. Patients are most often overweight. A majority of people with metabolic syndrome are overweight and lead a sedentary lifestyle. Lifestyle modification is the preferred treatment. Weight reduction usually requires a specifically tailored multifaceted program that includes diet and exercise. Sometimes medications or surgery may be useful.

(2) The nature of the invention and predictability in the art: The nature of the invention is therapeutic use of the inventive compounds to treat all these diseases/conditions. Dobrzyn, et al., Obesity Reviews 6, 169-174, 2005, at page 173, recognizes:

> Taken together, the findings reveal SCD to be a promising therapeutic target for the treatment of obesity, diabetes, liver steatosis and other metabolic diseases. However, the potential use of an SCD inhibitor as a human therapeutic agent awaits a more compete understanding of the mechanism underlying the effects of SCD deficiency and indication that the inhibition of this enzyme is both safe and efficacious.

It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: The direction and guidance provided is very limited. The dosage range information (pages 31-34, *inter alia*) is so meager, that it would require extensive experimentation to determine a specific dosage for a specific disease/condition, mode of administration and therapeutic regimen. Moreover, the

dosage is generic; the same for the many disorders covered by the specification. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for the various types of diseases/conditions claimed. *In vivo* testing is limited to mice, so claims 1 and 3, directed specifically to human use, have no teaching of how to use the invention.

(4) State of the Prior Art: Applicants do not provide highly predictive competent evidence or recognized tests to treat all conditions and other diseases recited for the inventive compounds. Pharmacological activity in general is unpredictable. In applications involving physiological activity, such as the present,

> "The first paragraph of 35 U.S.C. 112 effectively requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."

Plant Genetic Systems N.V. v. DeKalb Genetics Corp., 65 USPQ2d 1452, 1456 (Fed.Cir. 2003).

At present no known drug can successfully prevent or reverse the course of all conditions/diseases recited and encompassed by the present claims, despite the fact that many drugs are said to inhibit stearoyl-CoA desaturase activity. Substantiation of utility and its scope is required when utility is "speculative," "sufficiently unusual" or not provided. See *Ex parte Jovanovics, et al.*, 211 USPQ 907, 909 (BPAI 1981). Also, note *Hoffman v. Klaus*, 9 USPQ2d 1657 (BPAI 1988) and *Ex parte Powers*, 220 USPQ 924 (BPAI 1982) regarding types of testing needed to support *in vivo* uses.

See the discussion of Dobrzyn above. In addition, Giutiérrez-Juárez, et al., J. Clin. Invest., Vol. 116, No. 6, June 2006, pp. 1686-1695, at p. 1691, reports:

> In the effects of SCD1 deficiency are confirmed in humans, the pharmacological inhibition of this enzyme should have independent and beneficial effects on both weight gain and insulin action. SCD1 deficiency may also account for the lack of hepatic insulin resistance in several genetic models in which a primary alteration in other steps in hepatic lipid metabolism also leads to a secondary decrease in SCD1 expression.

Thus, the state of the prior art recognizes that the inhibition of stearoyl-CoA desaturase activity as an effective treatment of the specific diseases and conditions recited is an area for future research, especially as applied to human therapy.

(5) Working Examples: The specification provides enablement for inhibition of stearoyl-COA desaturase activity in mice (pages 31-35 and 50-52, *inter alia*) and claims directed thereto would be deemed allowable.

Although the specification refers to testing procedures, it is apparent that the only testing actually performed is with mice, because that is the only specific data reported. In addition, the specification tests offer no evidence establishing any connection between inhibition of stearoyl-COA desaturase activity in mice and any specific disease or condition recited in the claims, especially as applied to human patients. The stearoyl-COA desaturase activity testing in mice (pages 50-52, *inter alia*) provides no correlation between any specific compound of the present invention and inhibition of any specific disease or condition. There is no indication that the testing reported in the present specification is art-recognized.

(6) Skill of those in the art: The prior art recognizes that no compound has ever been capable of treating all diseases or conditions recited by the present claims generally.

Discussions above of the skill of those in the art support that successful treatment of diseases caused by and/or associated with stearoyl-CoA desaturase activity is a subject for further investigation, especially as applied to human patients.

(7) The quantity of experimentation needed: Based on the content of the disclosure, an undue burden would be placed on one skilled in the pharmaceutical arts to use the invention, since the disclosure gives the skilled artisan inadequate guidance regarding pharmaceutical use, for the reasons stated above.

The consideration of the above factors demonstrates that the present application sufficiently lacks enablement of the present claims. In view of the breath of the claims, the pharmaceutical nature of the invention, the unpredictability of relationship between stearoyl-CoA desaturase activity and specific conditions and diseases, one of ordinary skill in this art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states,

> A conclusion of lack of enablement means that, based on the evidence regarding each of the above [Wand] factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed.Cir. 1993).

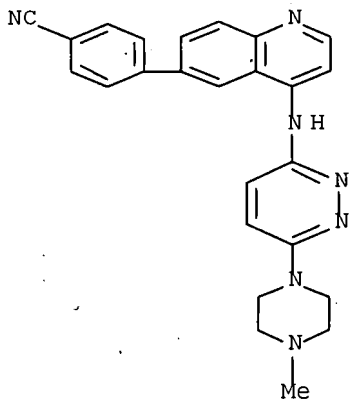
The above consideration justifies that conclusion here; undue experimentation would be required to practice Applicants' invention.

Rejections Under 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

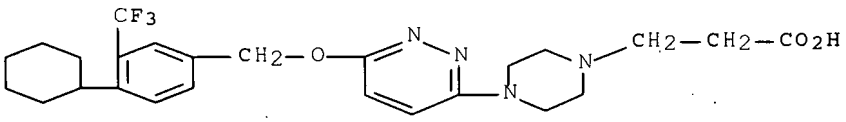
> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 10 and 37 are rejected under 35 U.S.C. 102(a) as anticipated by Dickson, et al., US 2006009460, entitled to the Jun. 4, 2004 priority date, describing RN 871873-26-6, Benzonitrile, 4-[4-[[6-(4-methyl-1-piperazinyl)-3-pyridazinyl]amino]-6-quinolinyl]-,



exhibiting ATP-utilizing enzyme inhibitory activity and useful for treatment of Alzheimer's disease, stroke, diabetes, obesity, inflammation, Crohn's disease, cancer, etc.

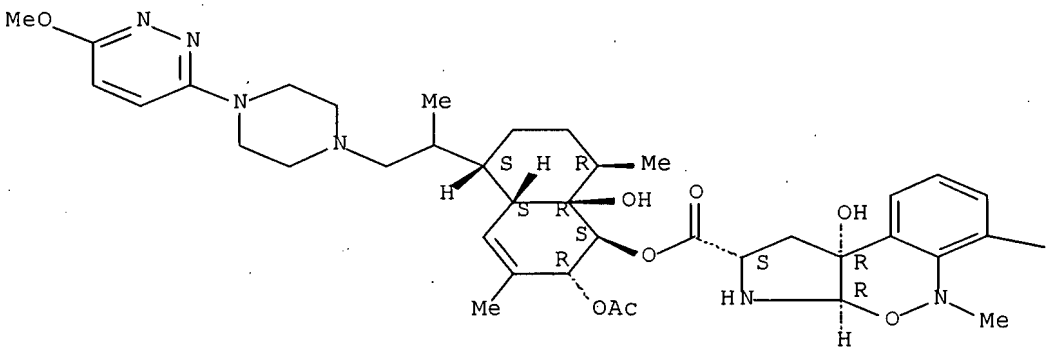
Claims 10 and 37 are rejected under 35 U.S.C. 102(a) as being anticipated by Lu, et al., US 2007203100, entitled to the priority date of Feb. 24, 2004, describing RN 864358-95-2, 1-Piperazinepropanoic acid, 4-[6-[[4-cyclohexyl-3-(trifluoromethyl)phenyl]methoxy]-3-pyridazinyl]-,



useful as immunosuppressants, particularly for diseases associated with EDG receptor mediated signal transduction.

Claims 10 and 37 are rejected under 35 U.S.C. 102(a) as being anticipated by Chubb, et al., US 2007185101, entitled to the priority date of Feb. 14, 2003, describing RN 745064-54-4, Pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylic acid, 6-chloro-1,2,3,3a,5,9b-hexahydro-9b-hydroxy-5-methyl-, (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-1,2,4a,5,6,7,8,8a-octahydro-8a-hydroxy-5-[2-[4-(6-methoxy-3-pyridazinyl)-1-piperazinyl]-1-methylethyl]-3,8-dimethyl-1-naphthalenyl ester, (2S,3aR,9bR)-,

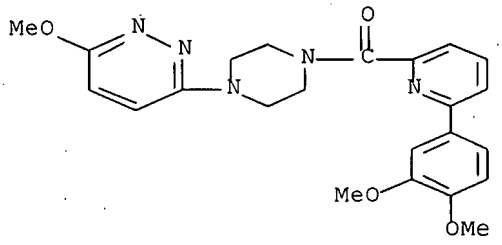
PAGE 1-A



, useful as a pharmaceutical antiparasitic agent.

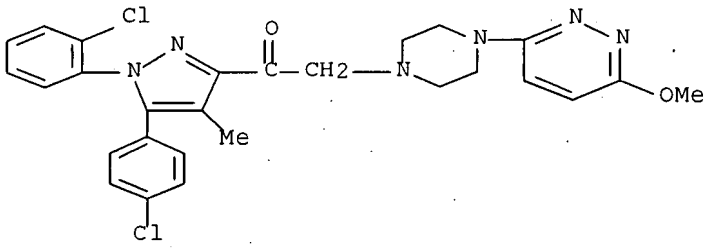
Claims 10, 11 and 37 are rejected under 35 U.S.C. 102(a) over Iwata, et al., JP 2004203871, published Jul 22, 2004, describing RN 479223-44-4, Piperazine, 1-[[6-

(3,4-dimethoxyphenyl)-2-pyridinyl]carbonyl]-4-(6-methoxy-3-pyridazinyl)-,



, which inhibited phosphodiesterase 4.

Claims 10 and 37 are rejected under 35 U.S.C. 102(a) as anticipated by Dow, et al., US 7247628, entitled to the priority date of Dec. 12, 2002, describing RN 709034-95-7, Ethanone, 1-[1-(2-chlorophenyl)-5-(4-chlorophenyl)-4-methyl-1H-pyrazol-3-yl]-2-[4-(6-methoxy-3-pyridazinyl)-1-piperazinyl]-,



, useful as cannabinoid CB1 receptor antagonists.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Database CAPLUS AN: 1968:95776 describing RN 18524-49-7, cited by Applicants.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Database CAPLUS AN: 1967:473577 describing RN 15567-65-4, cited by Applicants.

Claims 10, 11 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Iwata, et al., WO 02/102778, published Dec. 27, 2002, and EP 1396487, published Mar. 10, 2004, both cited by Applicants; see WO 02/102778, Example 49 at page 40 and EP 1396487, Example 49 at page 31.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Herron, et al., WO 02/10154, entitled to the priority date of Jul. 27, 2000, cited by Applicants; see Examples P13 – P21, 48, 52, 81, 85.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Pollak, et al., WO 99/00386, published Jan. 7, 1999, cited by Applicants; see Examples 5 & 7.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Earl, et al., US 5166147, issued Nov. 24, 1992, cited by Applicants; see Examples 8, 12.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Stokbroekx, et al., EP 0320032, published Jun. 14, 1989, cited by Applicants; see page 28, Examples 13, 14, 16; page 33, Example 30; page 34, Example 88.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Stokbroekx, et al., EP 0211457, published Feb. 25, 1987, cited by Applicants; see Examples 6, 9.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Stokbroekx, et al., EP 0156433, published Oct. 2, 1985, cited by Applicants; see Example 41.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Janssen, US 2985657, Issued May 23, 1961, cited by Applicants; see Examples 20, 24.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Van Emelen, et al., WO 03/076422, entitled to the priority date of Mar. 13, 2002, cited by Applicants; see Examples A21, B17, B24.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Boissier, J. Med. Chem., Vol. 6, Sep. 1963, 541-544, cited by Applicants; see pg. 542, Ex. XXIII.

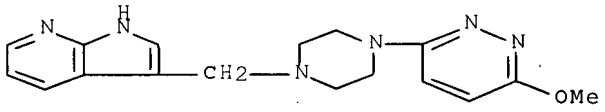
Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Ratouis, J. Med. Chem., Vol. 8, 1965, 104-107, cited by Applicants; see pg. 105, Ex. 38.

Claims 10, 11, 15 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Toldy, et al., Acta Chim. Acad. Scien. Hung., Vol. 49, No. 3, 1966, pgs. 265-286, cited by Applicants; see pg. 268, Ex. 15.

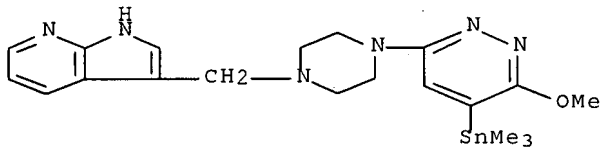
Claim 10 is rejected under 35 U.S.C. 102(b) as anticipated by Steck, et al., J. Het. Chem., Vol. 11, 1974, pgs. 1077-1079, cited by Applicants; see pg. 1079.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Hori, et al., Chem. Pharm. Bull., Vol. 29, No. 5, 1981, 1253-1266, cited by Applicants; see pg. 1259, Ex. 17x.

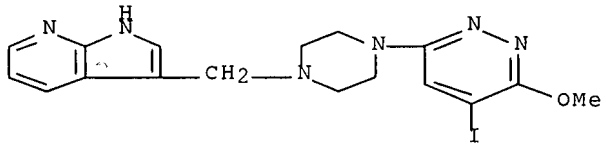
Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Pollak, et al., US 5976497, patented Nov. 2,1999, describing RN 219635-11-7, 1H-Pyrrolo[2,3-b]pyridine, 3-[[4-(6-methoxy-3-pyridazinyl)-1-piperazinyl]methyl]-,



RN 219635-16-2, 1H-Pyrrolo[2,3-b]pyridine, 3-[[4-[6-methoxy-5-(trimethylstannyl)-3-pyridazinyl]-1-piperazinyl]methyl]-,

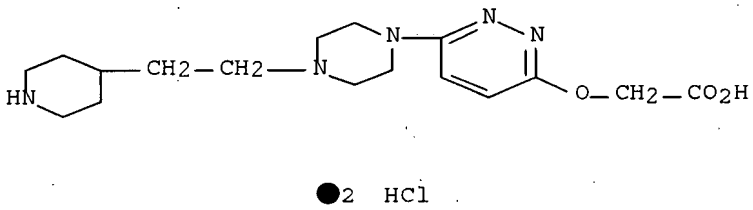


RN 219635-21-9, 1H-Pyrrolo[2,3-b]pyridine, 3-[[4-(5-iodo-6-methoxy-3-pyridazinyl)-1-piperazinyl]methyl]-,

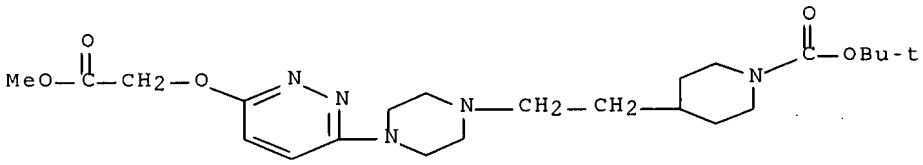


, as dopamine D4 receptor ligands.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Pieper, et al., US 5994356, Nov. 30, 1999, describing RN 198626-16-3, Acetic acid, [[6-[4-[2-(4-piperidinyl)ethyl]-1-piperazinyl]-3-pyridazinyl]oxy]-, dihydrochloride,



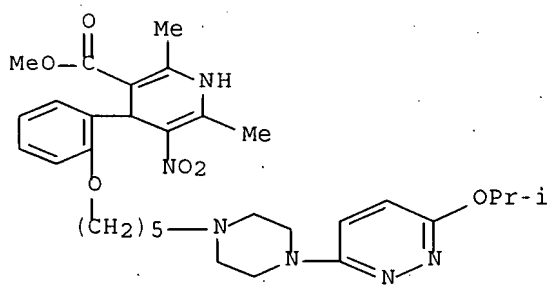
RN 198628-02-3, 1-Piperidinecarboxylic acid, 4-[2-[4-[6-(2-methoxy-2-oxoethoxy)-3-pyridazinyl]-1-piperazinyl]ethyl]-, 1,1-dimethylethyl ester,



, as cell aggregation inhibitors.

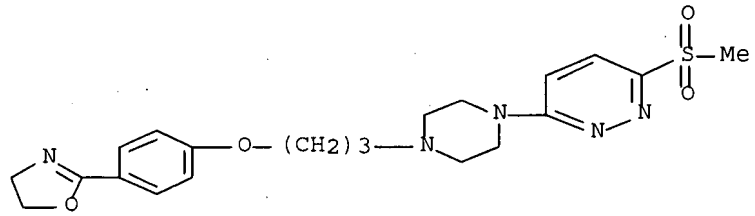
Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Earl, US 5166147, patented Nov. 24, 1992, describing RN 146825-54-9, 3-Pyridinecarboxylic

acid, 1,4-dihydro-2,6-dimethyl-4-[2-[[5-[4-[6-(1-methylethoxy)-3-pyridazinyl]-1-piperazinyl]pentyl]oxy]phenyl]-5-nitro-, methyl ester,



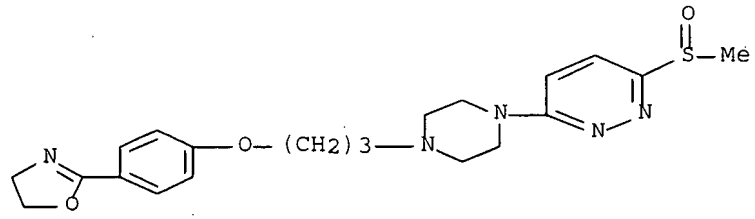
, for treating congestive heart failure.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Stokbroekx, et al., US 5106973, patented Apr. 21, 1992, describing RN 124436-73-3, Pyridazine, 3-[4-[3-[4-(4,5-dihydro-2-oxazolyl)phenoxy]propyl]-1-piperazinyl]-6-(methylsulfonyl)-,



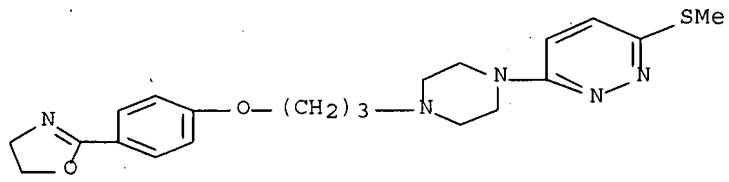
,

RN 124436-74-4, Pyridazine, 3-[4-[3-[4-(4,5-dihydro-2-oxazolyl)phenoxy]propyl]-1-piperazinyl]-6-(methylsulfinyl)-,

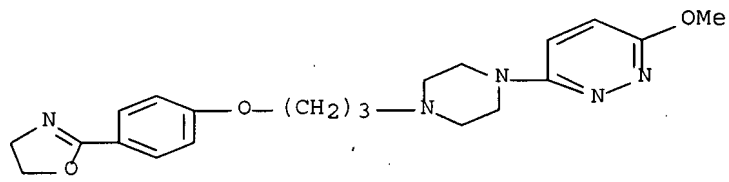


,

RN 124437-24-7, Pyridazine, 3-[4-[3-[4-(4,5-dihydro-2-oxazolyl)phenoxy]propyl]-1-piperazinyl]-6-(methylthio)-,

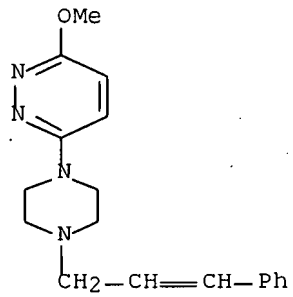


RN 124437-29-2, Pyridazine, 3-[4-[3-[4-(4,5-dihydro-2-oxazolyl)phenoxy]propyl]-1-piperazinyl]-6-methoxy-,

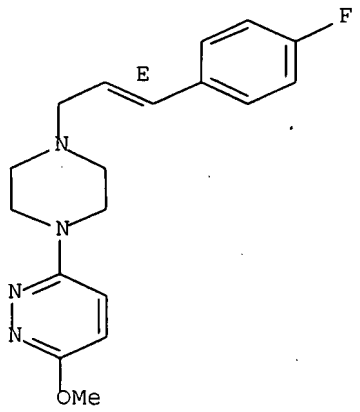


, as antiviral agents.

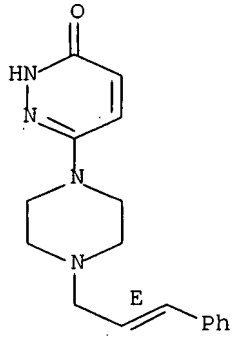
Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Janssen Pharmaceutica, JP 62029575, Feb. 7, 1987, describing RN 107746-69-0, Pyridazine, 3-methoxy-6-[4-(3-phenyl-2-propenyl)-1-piperazinyl]-,



RN 107746-75-8, Pyridazine, 3-[4-[3-(4-fluorophenyl)-2-propenyl]-1-piperazinyl]-6-methoxy-,

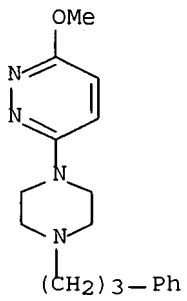


RN 107746-96-3, 3(2H)-Pyridazinone, 6-[4-(3-phenyl-2-propenyl)-1-piperazinyl]-,



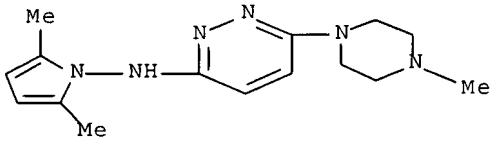
, as analgesics.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Stokbroekx, et al., US 5157035, patented Oct. 20, 1992, describing RN 100241-15-4, Pyridazine, 3-methoxy-6-[4-(3-phenylpropyl)-1-piperazinyl]-,



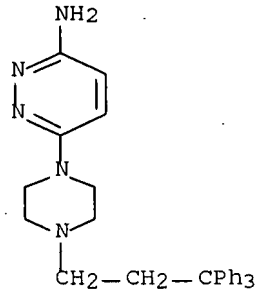
, as a virucide.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Bellasio, et al., Journal of Medicinal Chemistry (**1984**), 27(8), 1077-83, describing RN 75841-91-7, 3-Pyridazinamine, N-(2,5-dimethyl-1H-pyrrol-1-yl)-6-(4-methyl-1-piperazinyl)-,

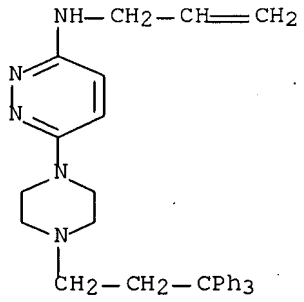


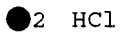
, having antihypertensive activity.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as anticipated by Regnier, et al., Journal of Medicinal Chemistry (**1972**), 15, 295-301, describing RN 36524-71-7, 3-Pyridazinamine, 6-[4-(3,3,3-triphenylpropyl)-1-piperazinyl]-,

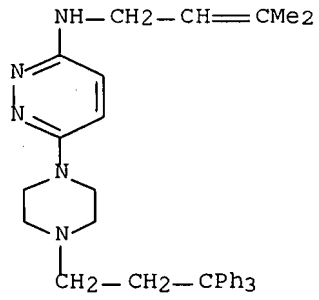


RN 36524-72-8, 3-Pyridazinamine, N-2-propenyl-6-[4-(3,3,3-triphenylpropyl)-1-piperazinyl]-, dihydrochloride,



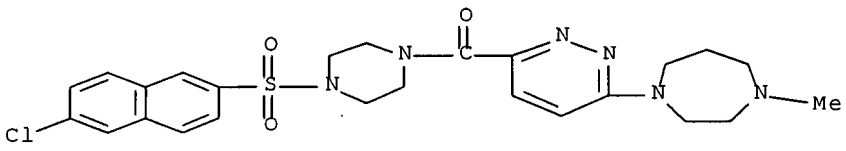


RN 36524-73-9, 3-Pyridazinamine, N-(3-methyl-2-butenyl)-6-[4-(3,3,3-triphenylpropyl)-1-piperazinyl]-,

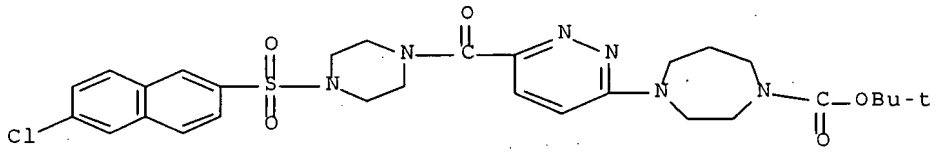


, as analgesics.

Claims 10 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Herron, et al., WO 2002010154, published Feb. 7, 2002, describing RN 395684-35-2, Piperazine, 1-[(6-chloro-2-naphthalenyl)sulfonyl]-4-[[6-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-3-pyridazinyl]carbonyl]-,



RN 395685-15-1, 1H-1,4-Diazepine-1-carboxylic acid, 4-[6-[[4-[(6-chloro-2-naphthalenyl)sulfonyl]-1-piperazinyl]carbonyl]-3-pyridazinyl]hexahydro-, 1,1-dimethylethyl ester,



, useful in the treatment of thromboembolic disorders.

Objected Claims – Allowable Subject Matter

Claims 12-14 and 16-35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 12-14 and 16-35 are seen to be directed to patentable subject matter, because the references of record do not show or suggest compounds having the particular combination of variables recited by these claims, particularly the exact combination of the bridging substituents W and V.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cecilia M. Jaisle, J.D. whose telephone number is 571-

272-9931. The examiner can normally be reached on Monday through Friday; 8:30 am through 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cecilia M. Jaisle, J.D.
9/11/2007

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